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EXAMINER

SASAN, ARADHANA

ART UNIT

PAPER NUMBER

1615

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/530,483	<b>Applicant(s)</b> ROSENBERG ET AL.	
	<b>Examiner</b> ARADHANA SASAN	<b>Art Unit</b> 1615	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 12 August 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                    | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

## DETAILED ACTION

### *Status of Application*

1. The remarks filed on 08/12/09 are acknowledged. No claims were amended.
2. Claims 1-22 are included in the prosecution.

### *Response to Arguments*

3. Please note that in the office action mailed 04/13/09, on Pages 2 and 3 (points 6-8), there was an inadvertent error. Each of these points stated that Applicant's arguments were fully considered and were persuasive. However, there was also a statement that "therefore, the rejection of 07/09/08 is maintained". This last statement should have been deleted since the arguments were persuasive and also since the office action included new grounds of rejection.

### MAINTAINED REJECTIONS:

The following is a list of maintained rejections:

### *Claim Rejections - 35 USC § 103*

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 1-4, 6-8, 10-19 and 21-22 **remain** rejected under 35 U.S.C. 103(a) as being unpatentable over Klimesch et al. (US 5,073,379) in view of Thacharodi et al. (EP 0 960 620 A1).

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The claimed invention is a process for producing solid dosage forms comprising forming a moldable cohesive composition which comprises:

- a) 50 to 99.4% by weight of at least one crosslinked nonthermoplastic carrier,
- b) 0.5 to 30% by weight of at least one adjuvant (selected from the group consisting of thermoplastic polymers, lipids, sugar alcohols, sugar alcohol derivatives and solubilizers) and
- c) 0.1 to 49.5% by weight of at least one active ingredient.

The moldable cohesive composition is formed by heating at a temperature at or above the softening point of the adjuvant, but at least 70°C, in a multi-screw extruder and subsequently cooled.

Klimesch teaches "a continuous process for the preparation of solid pharmaceutical forms by extruding a polymer melt containing the active compound and forming the still plastic extrudate between a belt and a roller or two belts" (Col. 1, lines 5-9). Klimesch teaches that "it is as a rule substantially more advantageous if the extruder is in the form of a conventional single-screw or multi-screw mixing extruder, so that premixing is unnecessary" (Col. 1, lines 31-34). "Shaping takes place directly after the extrusion process. The still plastic extrudate is passed, if necessary with the aid of a suitable guide channel ... through the shaping apparatuses ..." (Col. 1, lines 48-51). Klimesch teaches that "extrudable pharmaceutical mixtures are mixtures of one or more pharmaceutical active compounds with one or more auxiliaries which are conventionally used in the preparation of pharmaceutical tablets and are pasty and therefore extrudable due to the melting or softening of one or more components" (Col. 3, lines 1-

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6). Pharmacologically acceptable polymers such as polyvinylpyrrolidone (PVP) and copolymers of N-vinylpyrrolidone (NVP) and vinyl acetate are disclosed (Col. 3, lines 6-12). Example 3 discloses crosslinked PVP as a tablet disintegrant (Col. 6, lines 52-53). Pharmacologically acceptable plasticizers such as fatty acid esters are disclosed (Col. 3, lines 29-38). Conventional pharmaceutical auxiliaries such as silicates, stearic acid or its salts with magnesium, lactose, cereal starch, corn starch or potato starch are also disclosed (Col. 4, lines 30-36). Active compounds are disclosed as substances having a pharmaceutical action and a very low level of side effects, provided that they do not decompose under the processing conditions, and the concentration of the active compound may be from 0.1% to 95% (Col. 4, lines 57-68 and Col. 5, line 1 to Col. 6, line 3). Theophylline is the active compound used in examples 1-14 (Col. 6, line 23 to Col. 8, line 21). Example 3 discloses: "47.5 parts of a copolymer having a K value of 30 and consisting of 60% by weight of N-vinylpyrrolidone and 40% by weight of vinyl acetate, 2.5 parts of crosslinked PVP as a tablet disintegrant and 50 parts of theophylline were mixed and extruded in a twin-screw extruder. The temperatures of the five shots were each 120°C, and the die was at 130°C. The still plastic extrudate was pressed to give oblong tablets as in Example 1 (temperature of the double link belt: +15 °C). The tablets were stable to mechanical effects" (Col. 6, lines 49-59).

Klimesch does not expressly teach a high level (50-99.4%) of crosslinked nonthermoplastic carrier.

Thacharodi teaches a process for making a pharmaceutical composition which comprises "mixing together a substituted pyridylsulfinyl benzimidazole ... with a

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pharmaceutically acceptable carrier, the carrier comprising at least one polymer which is at least partially comprised of vinylpyrrolidone monomeric units, together with any optionally included pharmaceutically acceptable excipients" (Page 3, [0012]). The pharmaceutically acceptable carrier is present in an amount from about 10% to about 98% by weight of the total weight of the composition (Page 5, [0020]). Fatty acid glycerides may also be used as pharmaceutically acceptable carriers (Page 5, [0022]). The fatty acid glyceride is "heated to above its melting point and the liquid obtained [is] mixed with other ingredients of the composition to obtain granules" (Page 5, [0023]). Example 6 discloses the heating of fatty acid glycerides (AKOMED R at 13.33% and GELUCIRE at 6.67%) to 60°C. After cooling the fatty acid glycerides to 30°C, a blend of the active ingredient (omeprazole at 13.33%) and cross-linked polyvinylpyrrolidone (KOLLIDON CL-M at 66.67%) was granulated with the fatty acid glycerides (Page 7, [0037] and Table 7).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a process for the preparation of solid pharmaceutical forms by extruding a polymer melt containing the active compound and forming the still plastic extrudate between a belt and a roller or two belts, as taught by Klimesch, combine it with the process of making a granular pharmaceutical composition with a high percentage (10 to 98%) of a pharmaceutically acceptable carrier such as cross-linked polyvinylpyrrolidone (Kollidon CL-M), as taught by Thacharodi, and produce the instant invention.

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One of ordinary skill in the art would do this because the use of a high level of cross-linked polyvinylpyrrolidone (KOLLIDON CL-M at 66.67%) in a stable oral pharmaceutical composition is known in the art, as evidenced by Thacharodi (Page 7, [0037], Table 7 and Page 8, Tables 9 and 10). Combining prior art elements according to known methods to yield predictable results would have been obvious to one of ordinary skill in the art. Please see MPEP 2141.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 1, the limitation of the process of heating the components in a multi-screw extruder would have been obvious over the process of extruding a polymer melt containing the active compound and the multi-screw mixing extruder, as taught by Klimesch (Col. 1, lines 5-9 and Col. 1, lines 31-34). The limitation of forming a moldable cohesive composition would have been obvious over the plastic extrudate that was pressed to give oblong tablets (Col. 6, Example 3, lines 49-59). The limitation of the crosslinked nonthermoplastic carrier would have been obvious over the crosslinked PVP taught by Klimesch (Col. 6, Example 3, lines 52-53) and over the cross-linked polyvinylpyrrolidone (KOLLIDON CL-M at 66.67%), as taught by Thacharodi (Page 7, [0037] and Table 7). The percentage (50 to 99.4%) of the crosslinked nonthermoplastic carrier would have been obvious over the cross-linked

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polyvinylpyrrolidone (KOLLIDON CL-M) used at 66.67% in Example 6 by Thacharodi (Page 7, [0037] and Table 7). One with ordinary skill in the art would use a high percentage of the polymer which functions as a disintegrant in order to optimize the desired release rate of the chose active ingredient. One of ordinary skill in the art would increase the disintegrant level in order to increase the rate of disintegration of the composition. The limitation of the adjuvant would have been obvious over the 13.33% (calculated  $20\text{mg}/150\text{mg} = 13.33\%$  by weight) of AKOMED R (lipid component) in Example 6, as disclosed by Thacharodi (Page 7, [0037] and Table 7). The limitation of the active ingredient would have been obvious over the active compounds that may be from 0.1% to 95%, as taught by Klimesch (Col. 4, lines 57-68 and Col. 5, line 1 to Col. 6, line 3). The limitation of heating at a temperature at or above the softening point of the adjuvant, but at least at 70°C, would have been obvious over the polymeric binder that "must soften or melt at from 50 to 180° C., ... so that the mass is extrudable", as taught by Klimesch (Col. 3, lines 24-26). The limitation of the multi-screw extruder would have been obvious over the advantageous multi-screw mixing extruder taught by Klimesch (Col. 1, lines 30-35). The limitation of subsequently cooling the moldable composition would have been obvious over the pressing of the extrudate to give oblong tablets "using a double link belt which was cooled to 15° C", as taught by Klimesch (Col. 6, lines 30-32).

Regarding instant claim 2, the limitation of the weight percentage of the crosslinked nonthermoplastic carrier would have been obvious over the cross-linked polyvinylpyrrolidone (KOLLIDON CL-M) used at 66.67% in Example 6 by Thacharodi

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(Page 7, [0037] and Table 7). The limitation of 5 to 30% of a thermoplastic carrier would have been obvious over the pharmaceutically acceptable carrier (present in an amount from about 10% to about 98%) comprising at least one polymer which is at least partially comprised of vinylpyrrolidone monomeric units, as taught by Thacharodi (Page 3, [0012]). The limitation of 0.5 to 20% of a solubilizer would be obvious over the solubilizers AKOMED R (caprylic/capric triglyceride at 13.33%) and GELUCIRE (glycerol esters of C<sub>8</sub>-C<sub>18</sub> fatty acids at 6.67%) as taught by Thacharodi (Page 7, [0037] and Table 7). The limitation of 0.1 to 45.5% of at least one active ingredient would have been obvious over the active compounds that may be from 0.1% to 95%, as taught by Klimesch (Col. 4, lines 57-68 and Col. 5, line 1 to Col. 6, line 3) and over the 13.33% of active (omeprazole at 13.33%) taught by Thacharodi (Page 7, [0037] and Table 7).

Regarding instant claim 3, the crosslinked nonthermoplastic carrier would have been obvious over the crosslinked PVP taught by Klimesch (Col. 6, Example 3, lines 52-53) and the cross-linked PVP taught by Thacharodi (Page 7, [0037] and Table 7).

Regarding instant claim 4, the thermoplastic polymer would have been obvious over the copolymers of N-vinylpyrrolidone (NVP) and vinyl acetate, as taught by Klimesch (Col. 3, lines 6-12).

Regarding instant claim 6, the lipid would have been obvious over the fatty acid esters (Col. 3, lines 29-38) and stearic acid (Col. 4, lines 30-36) as taught by Klimesch and over the AKOMED R (lipid component) in Example 6, as disclosed by Thacharodi (Page 7, [0037] and Table 7).

Regarding instant claim 7, the solubilizer would have been obvious over the fatty acid esters taught by Klimesch (Col. 3, lines 29-38) and over the solubilizers AKOMED R (caprylic/capric triglyceride at 13.33%) and GELUCIRE (glycerol esters of C<sub>8</sub>-C<sub>18</sub> fatty acids at 6.67%) taught by Thacharodi (Page 7, [0037] and Table 7).

Regarding instant claim 8, the limitation of the solubility of the active ingredient would have been obvious over the active compounds taught by Klimesch which include poorly water-soluble drugs such as betamethasone and acetylsalicylic acid (Col. 4, lines 57-68 and Col. 5, line 1 to Col. 6, line 3).

Regarding instant claim 10, the limitation of the tableting aid would have been obvious over the conventional pharmaceutical auxiliaries such as silicates, stearic acid or its salts with magnesium, lactose, cereal starch, corn starch or potato starch disclosed by Klimesch (Col. 4, lines 30-36).

Regarding instant claims 11-13, the limitations of components a) – c) that are mixed before heating, during heating and after heating would have been obvious over the process of mixing and extruding the components of the composition taught by Klimesch (Col. 6, lines 49-59). One with ordinary skill in the art would do this because during the process of routine experimentation the order of mixing and heating can be manipulated in order to achieve the desired attributes of the finished dosage form.

Regarding instant claim 14, the limitation of the moldable cohesive composition that is homogenized to distribute the active ingredient would have been obvious over the process of mixing and extruding the components of the composition taught by Klimesch (Col. 6, lines 49-59). One with ordinary skill in the art would ensure that the

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active ingredient was uniformly distributed in the composition by the process of mixing and extruding.

Regarding instant claim 15, the limitation of melting the adjuvant with the nonthermoplastic carrier and admixing the active ingredient would have been obvious over the process of extruding taught by Klimesch (Col. 6, lines 49-59) because during the process of routine optimization one with ordinary skill in the art would modify the order to adding the active ingredient to the other components in order to ensure uniformity.

Regarding instant claims 16-17, the residence time would have been obvious over the extrusion process taught by Klimesch (Col. 6, lines 49-59) because the residence time is a manipulatable parameter and one with ordinary skill in the art would increase or decrease the residence time of the composition in the multi-screw extruder during the process of routine experimentation. The recited residence time frames would have been obvious variants unless there is evidence of criticality or unexpected results.

Regarding instant claim 18, the limitations of shaping the molded cohesive composition between at least one belt and at least one roll would have been obvious over the extrusion of a polymer melt containing an active compound and forming the still plastic extrudate between a belt and a roller or two belts, as taught by Klimesch (Col. 1, lines 5-9).

Regarding instant claim 19, the limitations of shaping the molded cohesive composition by calendaring would have been obvious over the calendaring taught by Klimesch (Col. 1, lines 10-12).

Regarding instant claim 21, the limitation of the temperature range from 70°C - 180 °C, would have been obvious over the polymeric binder that "must soften or melt at from 50 to 180° C., ... so that the mass is extrudable", as taught by Klimesch (Col. 3, lines 24-26).

Regarding instant claim 22, the limitation of the process that is carried out in the absence of a solvent would have been obvious over the process where the active is sparingly soluble in water and forms a molecular disperse phase in the polymer melt without the addition of solvents, as taught by Klimesch (Col. 12, claim 14).

### ***Response to Arguments***

6. Applicant's arguments, see Page 2, filed 08/12/09, with respect to the rejection of claims 1-4, 6-8, 10-19 and 21-22 under 35 U.S.C. 103(a) as being unpatentable over Klimesch et al. (US 5,073,379) in view of Thacharodi et al. (EP 0 960 620 A1) have been fully considered but are not persuasive.

Applicant argues that: "A person of ordinary skill in the art will readily appreciate that the cross-linked, non-thermoplastic carrier which is employed in accordance with applicants' procedure cannot be softened or molten under the conditions required by Klimesch et al., and that cross-linked PVP which is mentioned in both references as a disintegrant<sup>3)</sup> decomposes upon heating prior to melting. Accordingly, no glass transition temperature can be measured for cross-linked, non-thermoplastic PVP The enclosed copy of a publication of Saavedra et al., for example, states: "The measured decomposition temperature was 367°C, so Tg [the glass transition temperature] for crosslinked PVP could be higher than this value."<sup>4)</sup> As pointed out in the foregoing,

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Klimesch et al. require that the glass transition temperature of the extruded mixture must in any case be less than 180°C and preferably less than 130°C. On the basis of the information which is provided by Klimesch et al., it is therefore not deemed to be obvious to a person of ordinary skill in the pertinent art to increase the amount of any non-thermoplastic material(s) beyond the at most 1:1 auxiliaries to polymeric binder ratio which is taught in the primary reference.”

Applicant argues that: “The information which is given in the disclosure of Thacharodi et al. is not deemed to render the result of such an extrusion predictable, or to suggest or imply that such an extrusion may reasonably be expected to be successful. Thacharodi et al. employ polymers which comprise vinyl-pyrrolidone monomeric units as stabilizing excipients for substituted pyridylsulfinyl benzimidazoles.<sup>6)</sup> In this context [it] is thus the presence of the pyrrolidone moieties which determine the suitability of the polymer for the purposes of Thacharodi et al.'s disclosure and not the thermoplastic properties which are required in the context of Klimesch et al.'s process.”

This is not persuasive because crosslinked polyvinylpyrrolidone is disclosed by Klimesch in the mixture comprising the active ingredient that is extruded, i.e., the crosslinked PVP is **extrudable** (with the die temperature of 100°C) (Klimesch, Col. 6, Example 1). Thacharodi also teaches cross-linked polyvinylpyrrolidone in a mixture with an active ingredient but at a higher level of cross-linked polyvinylpyrrolidone (Thacharodi, Page 7, Example 6). One of ordinary skill in the art would find it obvious to use the higher level of crosslinked PVP in the extrudable composition of Klimesch

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based on the teaching by Thacharodi that "because of its high swelling ability, cross-linked polyvinylpyrrolidone is conventionally used as a disintegrant in tablets; however, in the present invention it is used as a stabilizing excipient and as a diluent for the substituted pyridylsulfinyl benzimidazole" (Page 4, [0018], lines 55-57). One of ordinary skill in the art would know that crosslinked PVP is extrudable and can be used as either a disintegrant (due to its swelling ability), or as a stabilizer, or as a diluent. One of ordinary skill in the art would know that the amount of diluents in pharmaceutical formulations comprising active ingredients is in quantity sufficient amounts and can be modified based on the desired functionality of the diluent. Therefore, since the crosslinked PVP functions as a disintegrant/stabilizer/diluent, one of ordinary skill in the art would find it obvious to modify the level based on the desired function, i.e., high level for diluent and fast disintegration, low level for slower disintegration. Thacharodi clearly teaches a high level of crosslinked PVP in Example 6 and this reference is properly combined with Klimesch because it is obvious to combine prior art elements according to known methods to yield predictable results. Please see MPEP 2141.

Therefore, the rejection of 04/13/09 is maintained.

***Claim Rejections - 35 USC § 103***

7. Claim 5 **remains** rejected under 35 U.S.C. 103(a) as being unpatentable over Klimesch et al. (US 5,073,379) in view of Thacharodi et al. (EP 0 960 620 A1) and further in view of Endicott et al. (US 3,087,860).

The teachings of Klimesch and Thacharodi are stated above.

Klimesch and Thacharodi do not expressly teach sugar alcohols as adjuvants.

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Endicott teaches adjuvants such as sorbitol and mannitol (Col. 3, lines 67-70) and teaches that a drug-plastic combination can be mixed and extruded (Col. 4, lines 21-23).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a process for the preparation of solid pharmaceutical forms by extruding a polymer melt containing the active compound and forming the still plastic extrudate between a belt and a roller or two belts, as taught by Klimesch, combine it with the process of making a granular pharmaceutical composition with a high percentage (10 to 98%) of a pharmaceutically acceptable carrier such as cross-linked polyvinylpyrrolidone (Kollidon CL-M), as taught by Thacharodi, further combine it with the use of adjuvants such as sorbitol and mannitol in an extrudable drug/plastic composition, as taught by Endicott, and produce the instant invention.

One of ordinary skill in the art would have done this because sugar alcohols such as sorbitol and mannitol are known in the art to be used as excipients or adjuvants and can be included in extrudable compositions, as evidenced by the teaching of Endicott.

Regarding instant claim 5, the limitation of the sugar alcohol would have been obvious over the sorbitol and mannitol taught by Endicott (Col. 3, lines 67-70).

### ***Response to Arguments***

8. Applicant's arguments, see Page 5, filed 08/12/09, with respect to the rejection of claim 5 under 35 U.S.C. 103(a) as being unpatentable over Klimesch et al. (US 5,073,379) in view of Thacharodi et al. (EP 0 960 620 A1) and further in view of Endicott et al. (US 3,087,860) have been fully considered but are not persuasive.

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Applicant argues that: “the disclosure of Endicott et al. is unsuited to render the result of a modification of Klimesch et al.'s process on the basis of the disclosure of Thacharodi et al. predictable, or to supplement the necessary reasonable expectation of success for such a modification. The mere fact that Endicott et al. show sugar alcohols to be excipients or adjuvants for pharmaceutical compositions is not deemed to be sufficient to render the subject matter of applicants' Claim 5 as a whole obvious within the meaning of Section 103(a).”

This is not persuasive because Endicott teaches adjuvants such as sorbitol and mannitol (Col. 3, lines 67-70) and teaches that a drug-plastic combination can be mixed **and extruded** (Col. 4, lines 21-23). Since the mixture of drugs and adjuvants (sorbitol and mannitol) and an **extrudable** combination is disclosed, one of ordinary skill in the art would find it obvious to combine it with the teaching of Endicott with the drug-plastic extrusion teaching of Klimesch.

Therefore, the rejection of 04/13/09 is maintained.

### ***Claim Rejections - 35 USC § 103***

9. Claims 9 and 20 **remain** rejected under 35 U.S.C. 103(a) as being unpatentable over Klimesch et al. (US 5,073,379) in view of Thacharodi et al. (EP 0 960 620 A1) and further in view of Goertz et al. (US 4,801,460).

The teachings of Klimesch and Thacharodi are stated above.

Klimesch and Thacharodi do not expressly teach the cooled composition that is comminuted and compressed to the dosage form.

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Goertz teaches a process for the preparation of solid pharmaceutical forms by mixing one or more pharmaceutical active compounds with one or more fusible, pharmacologically tolerated binders and subjecting the mixture to extrusion and shaping, wherein the fusible binder used is a solvent-free NVP polymer (Col. 1, line 64 to Col. 2, line 4). "Shaping may be effected by injection molding or by extrusion followed by shaping of the plastic extrudate, for example by hotface cutting to give granules or molding to give tablets ... cold-face cutting is also suitable and may be followed by pressing of the granules to give tablets" (Col. 5, lines 11-20).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a process for the preparation of solid pharmaceutical forms by extruding a polymer melt containing the active compound and forming the still plastic extrudate between a belt and a roller or two belts, as taught by Klimesch, combine it with the process of making a granular pharmaceutical composition with a high percentage (10 to 98%) of a pharmaceutically acceptable carrier such as cross-linked polyvinylpyrrolidone (Kollidon CL-M), as taught by Thacharodi, further combine it with the cold-face cutting to give granules, as taught by Goertz, and produce the instant invention.

One of ordinary skill in the art would have done this because Goertz teaches the formation of tablets from the granules.

Regarding instant claim 9, the limitation of the cooled composition that is comminuted and compressed to the dosage form would have been obvious over the

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granules formed from the extruded composition, as taught by Goertz (Col. Col. 5, lines 11-20).

Regarding instant claim 20, the limitation of hot or cold cutting to form small-particle granules would have been obvious over the hot or cold cutting to form granules of the extruded composition, as taught by Goertz (Col. Col. 5, lines 11-20).

### ***Response to Arguments***

10. Applicant's arguments, see Page 5, filed 08/12/09, with respect to the rejection of claim 5 under 35 U.S.C. 103(a) as being unpatentable over Klimesch et al. (US 5,073,379) in view of Thacharodi et al. (EP 0 960 620 A1) and further in view of Goertz et al. (US 4,801,460) have been fully considered but are not persuasive.

Applicant argues that: "nothing in the disclosure of Goertz et al. suggests or implies that a composition comprising non-thermoplastic, crosslinked carriers in the amounts mandated by applicants' claims may be extruded successfully. In fact, similar to the teaching of Klimesch et al., Goertz et al. limit the total amount of pharmaceutical auxiliaries, including i.e. disintegrants, to 100% based on the amount of polymer binder.<sup>10)</sup> As such, the disclosure of Goertz et al. is also not deemed to be suited to render the result of a modification of Klimesch et al.'s process on the basis of the disclosure of Thacharodi et al. predictable, or to supplement the necessary reasonable expectation of success for such a modification. The mere fact that Goertz et al. mention cold-face cutting and pressing the granules into tablets cannot be considered sufficient to render the subject matter of applicants' Claims 9 and 20 as a whole obvious within the meaning of Section 103(a)."

This is not persuasive because Thacharodi teaches the high level of crosslinked PVP in granular formulations and one of ordinary skill in the art would look to Goertz for the formation of tablets from granules. These references are properly combined with Klimesch because Goertz teaches the shaping of the plastic **extrudate or granules** (which can be achieved by cold-face cutting). The limitations of the extrusion, the high level of crosslinked nonthermoplastic carrier and the comminution of the cooled composition are therefore rendered obvious by the combination of Klimesch, Thacharodi, and Goertz.

Therefore, the rejection of 04/13/09 is maintained.

### ***Conclusion***

11. No claims are allowed.
12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

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13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax, can be reached at 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/  
Examiner, Art Unit 1615

/Robert A. Wax/  
Supervisory Patent Examiner, Art Unit 1615